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Total Synthesis of Viridin and Viridiol

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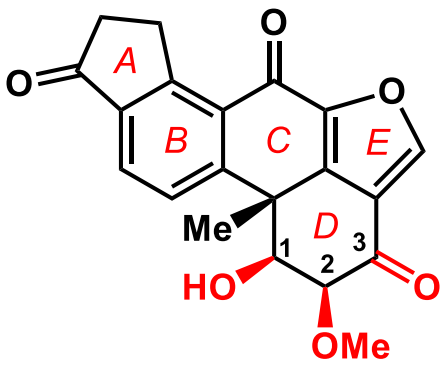
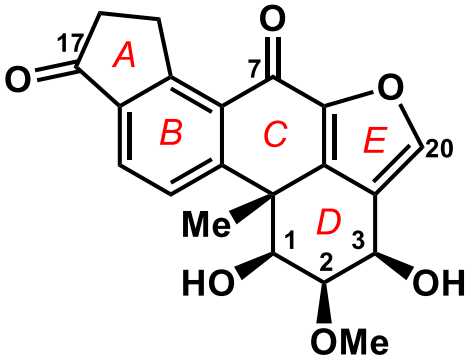
Supporting Information

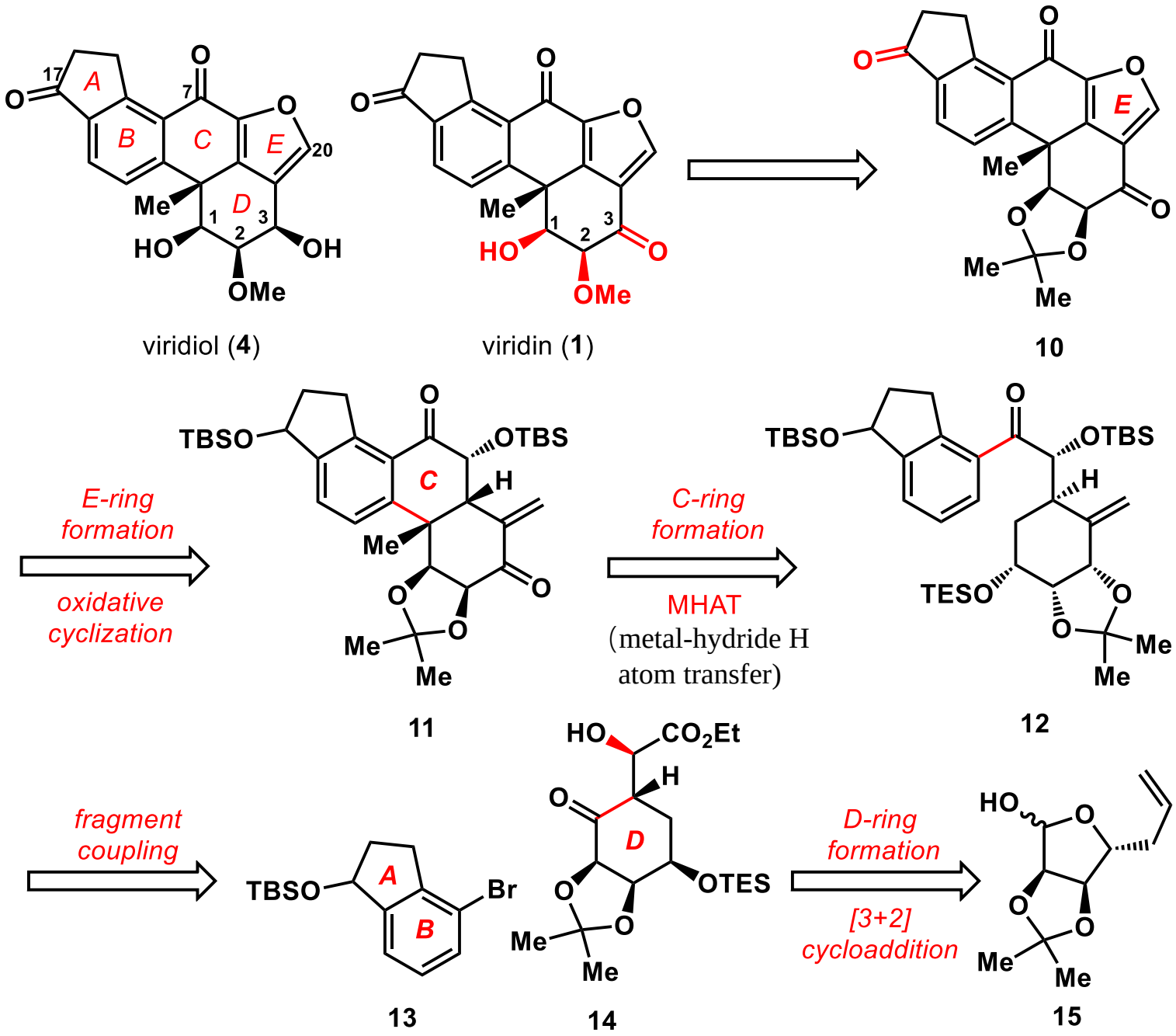


viridin (**1**)

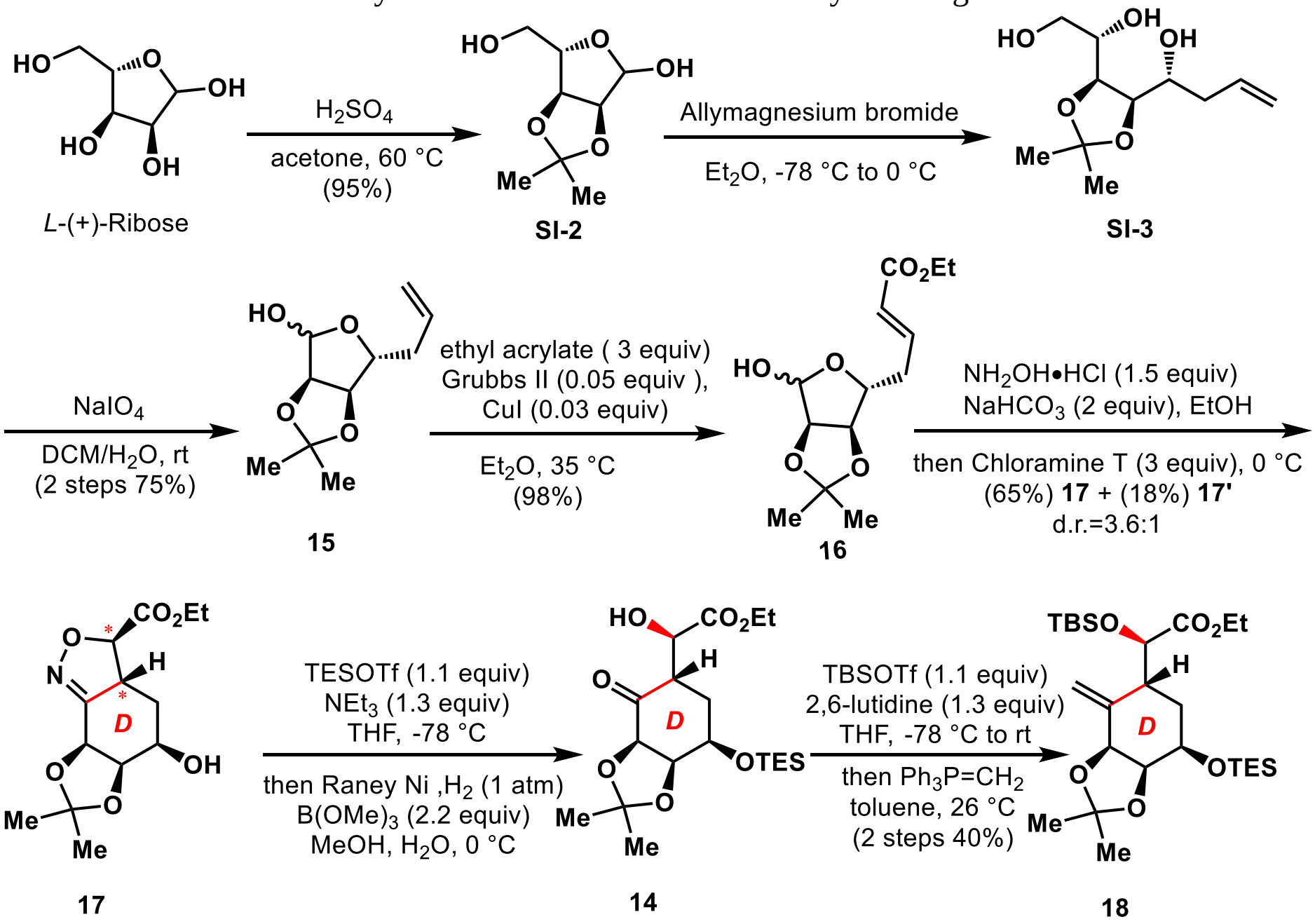


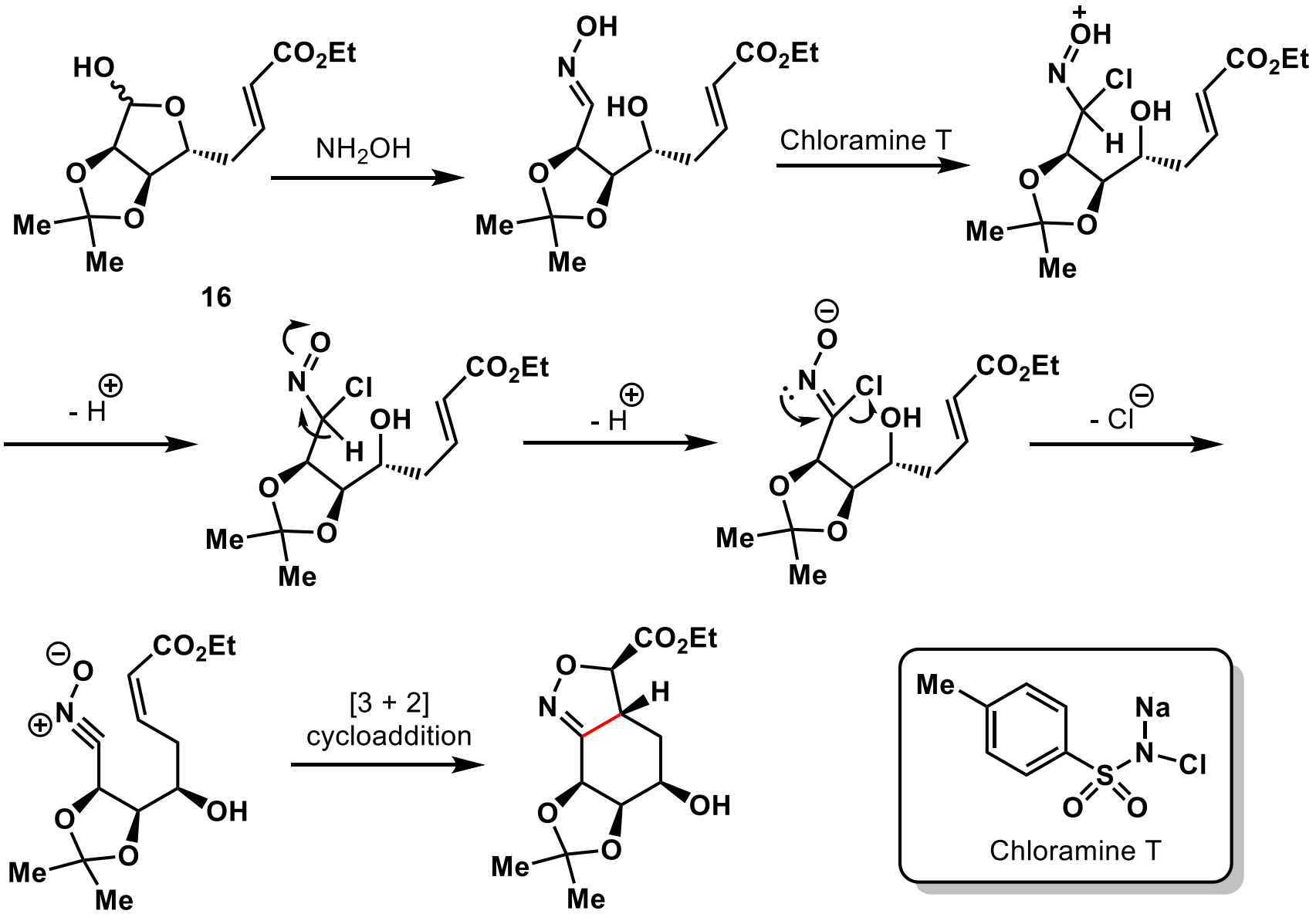
viridiol (**4**)

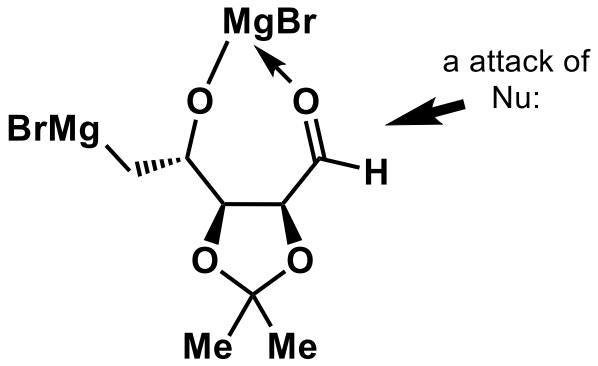
Scheme 1. Retrosynthetic Analysis of Viridin



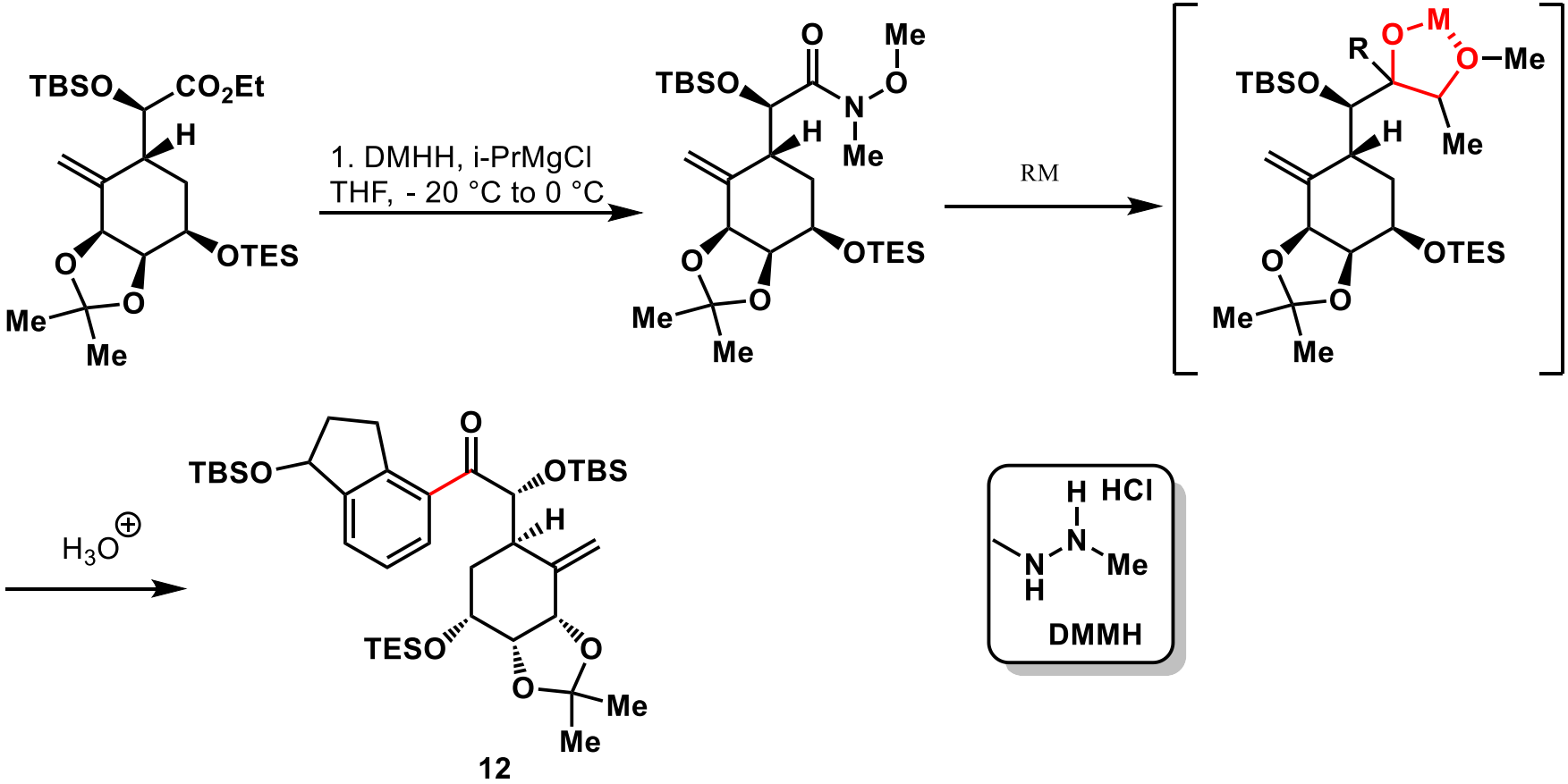
Scheme 2. MHAT Radical Cyclization To Construct the Tetracyclic Ring

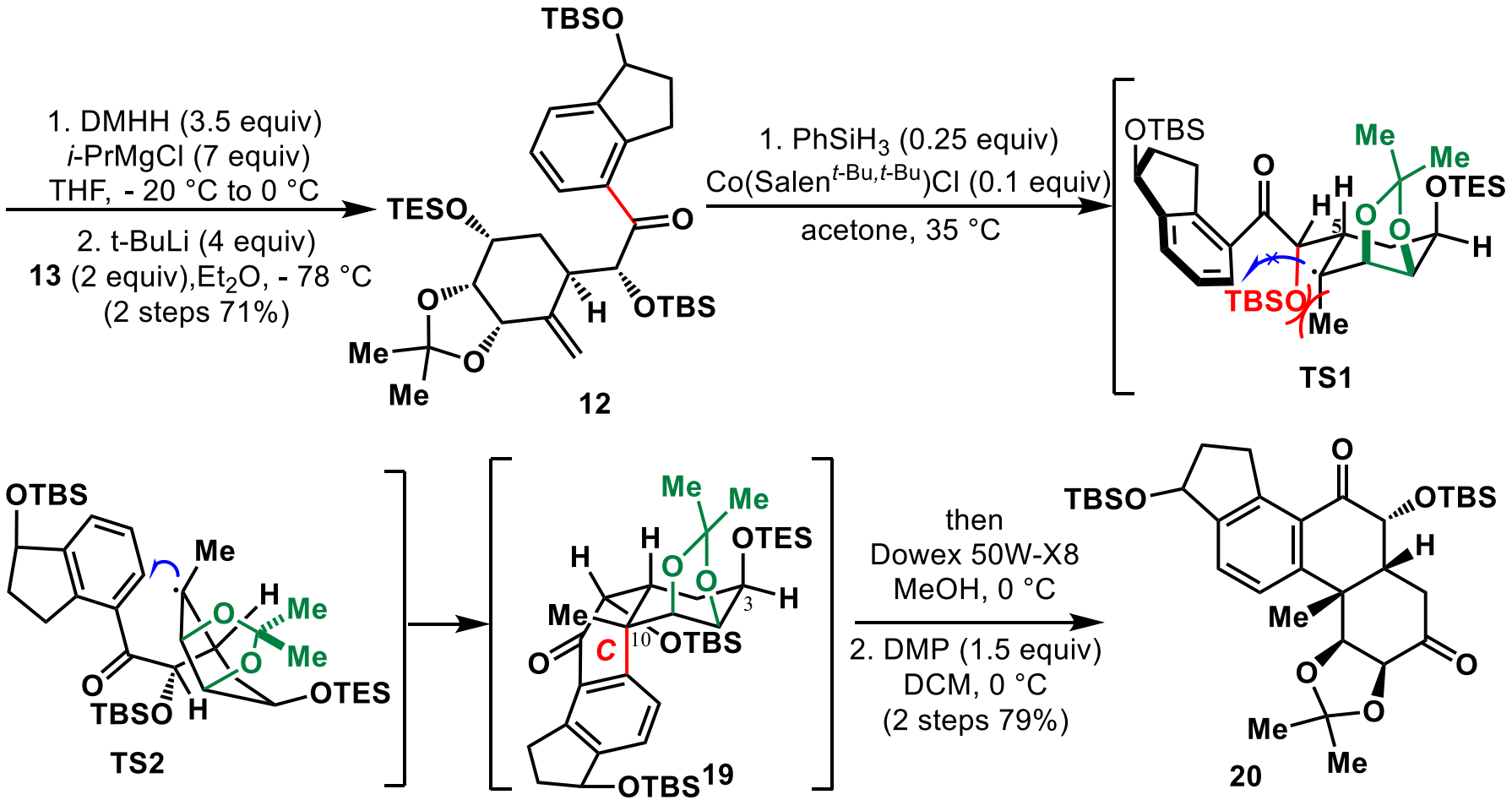


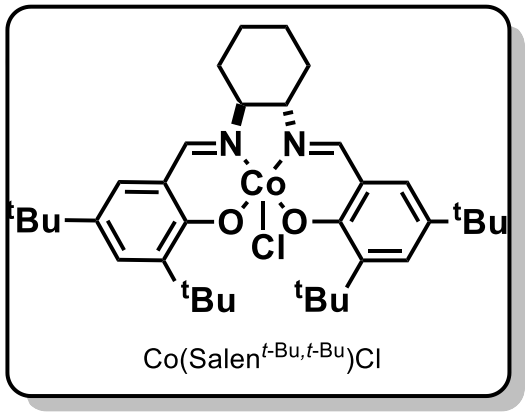

HO
CO2Et
O
O
Me
Me
16
NH2OH
OH
N
HO
CO2Et
Chloramine T
OH
N
Cl
OH
H
CO2Et
- H
O
N
Cl
OH
H
CO2Et
- H
O
N
Cl
OH
CO2Et
- Cl
[3 + 2]
cycloaddition
CO2Et
O
N
H
OH
Me
Na
N
Cl
S
O
O
Chloramine T

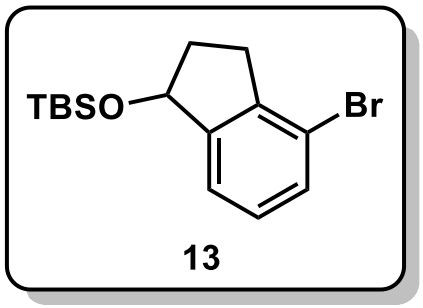


Chelation transition model

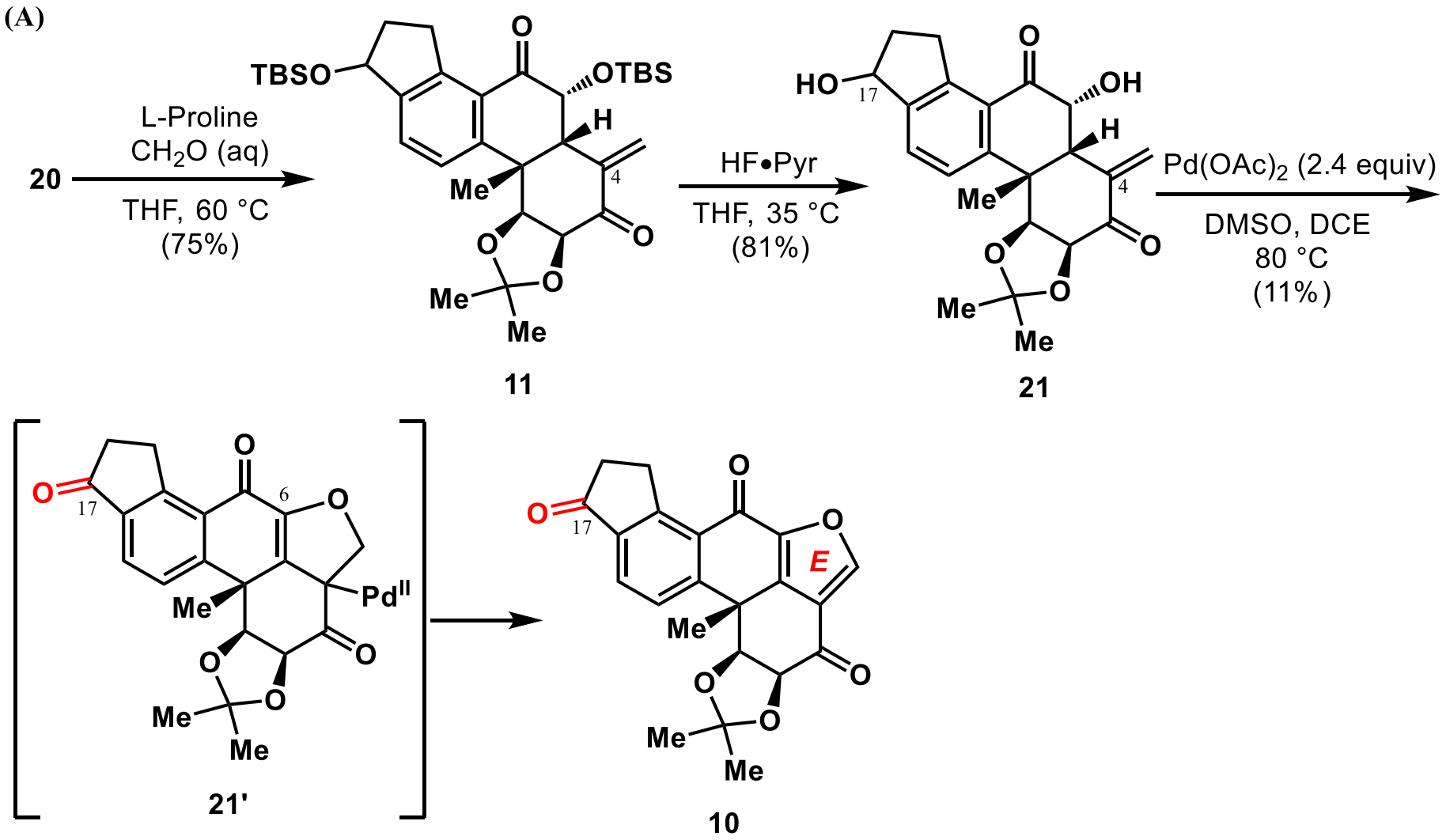



1. DMHH (3.5 equiv)
i-PrMgCl (7 equiv)
THF, - 20 °C to 0 °C
2. t-BuLi (4 equiv)
13 (2 equiv),Et2O, - 78 °C
(2 steps 71%)
12
1. PhSiH3 (0.25 equiv)
Co(Salen t-Bu,t-Bu)Cl (0.1 equiv)
acetone, 35 °C
TS1
TS2
19
then
Dowex 50W-X8
MeOH, 0 °C
2. DMP (1.5 equiv)
DCM, 0 °C
(2 steps 79%)
20

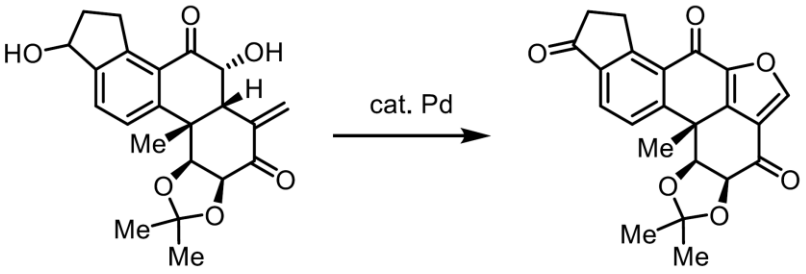

Co(Salen t-Bu,t-Bu)Cl


13

Scheme 3. Total Synthesis of Viridin and Viridiol



Screening of the Pd-promoted dehydrogenation-cyclization condition:

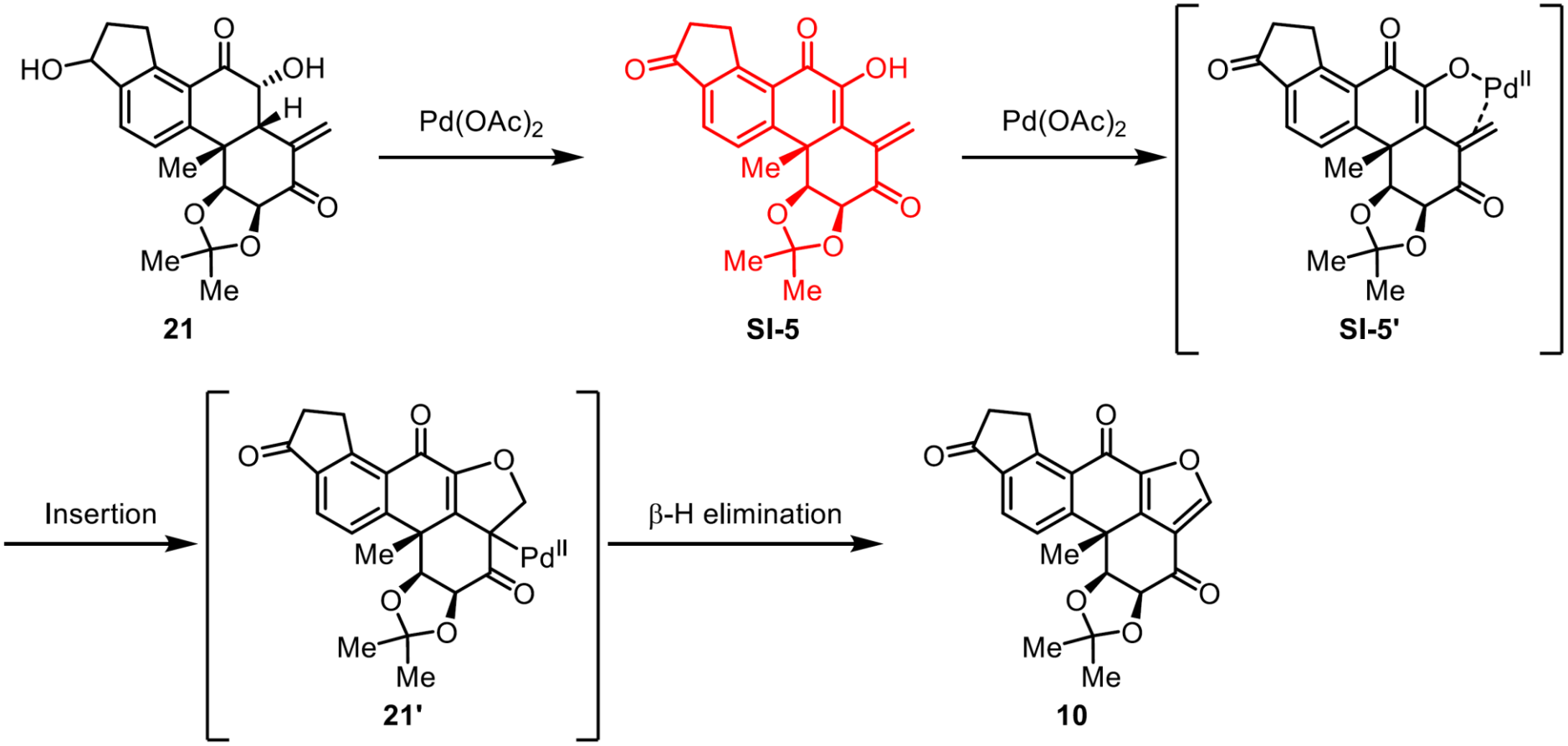


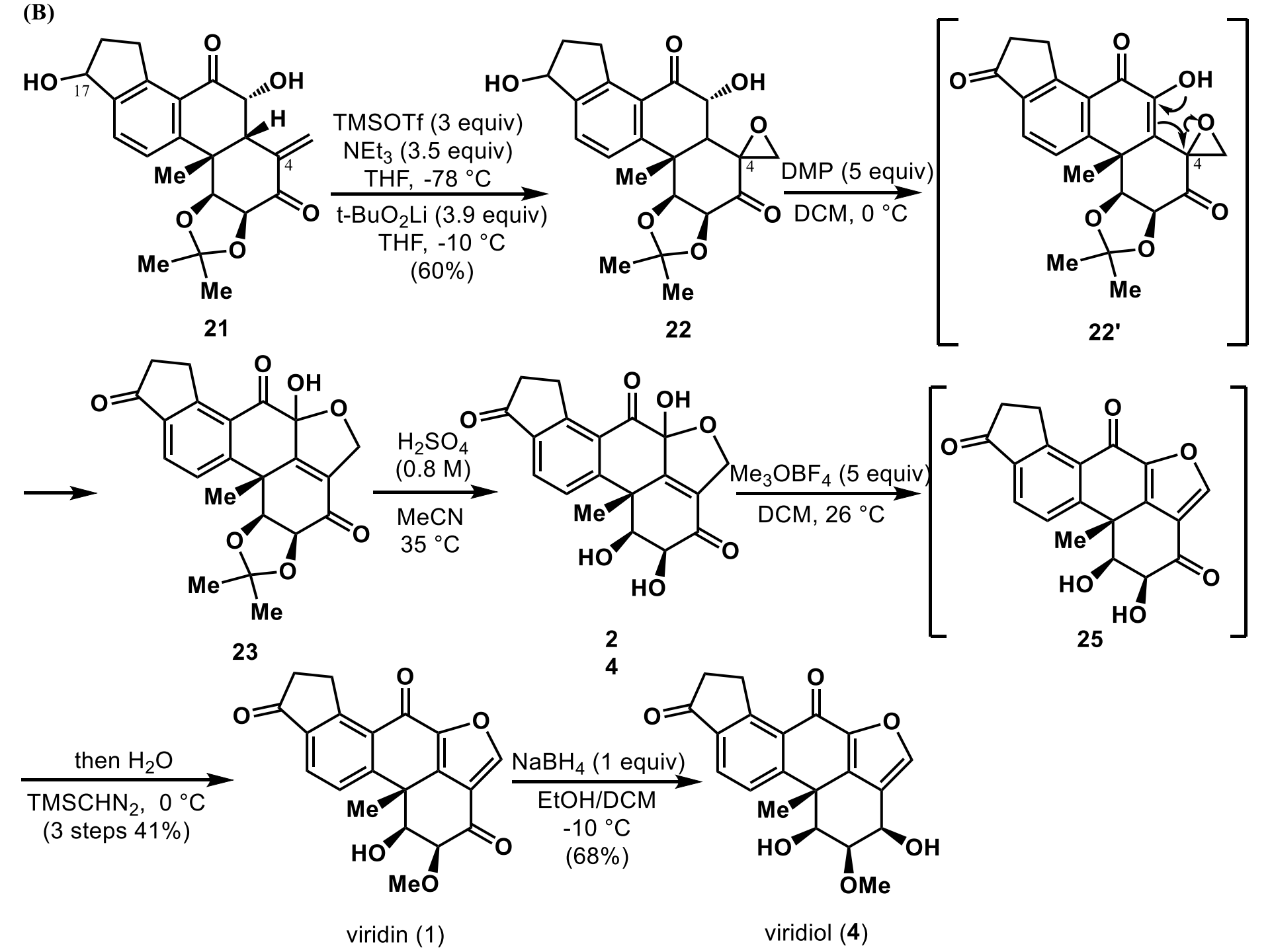
21 **10**

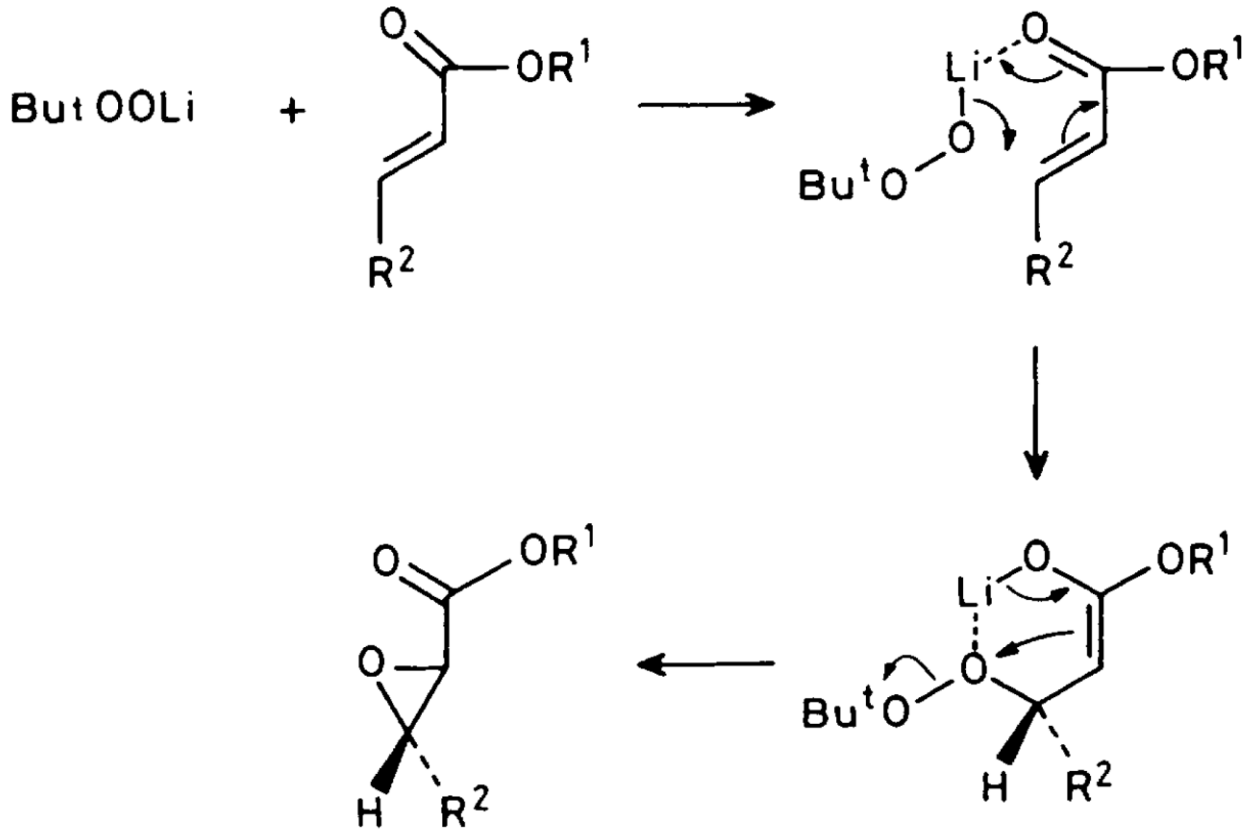
entry	Pd	solvent	additive [c]	T. (°C)	time (h)	result
1[a]	$Pd(OAc)_2$	DMSO	-	80	2	**10** (trace)
2[a]	$PdCl_2$	DMSO	-	80	24	N.R.
3[a]	$Pd(TfA)_2$	DMSO	-	80	4	decompose
4[b]	$Pd(OAc)_2$	DMSO	-	80	2	**10** (trace)
5[b]	$Pd(OAc)_2$	DMSO	-	40	12	N.D.
6[b]	$Pd(OAc)_2$	toluene	-	80	12	complex
7[b]	$Pd(OAc)_2$	DCE	-	80	2	**10** (trace)
8[b]	$Pd(OAc)_2$	cyclohexane	-	80	12	N.D.
9[b]	$Pd(OAc)_2$	MeCN	-	80	2	**10** (trace)
10[b]	$Pd(OAc)_2$	DMF	-	80	0.5	decompose
11[b]	$Pd(OAc)_2$	DCE	-	80	4	**10** (trace)
12[b]	$Pd(OAc)_2$	1,4-Dioxane	-	80	2	N.D.
13[b,c]	$Pd(OAc)_2$	DCE	$CaCO_3$	80	12	**10** (trace)
14[b,c]	$Pd(OAc)_2$	DCE	Ag_2CO_3	80	12	**10** (trace)
15[b,c]	$Pd(OAc)_2$	DCE	Ag_2O	80	22	N.D.
16[b,c,d]	$Pd(OAc)_2$	DCE	DMSO	80	2.5	**10** (5%)
17[b,c,e]	$Pd(OAc)_2$	DCE	DMSO	80	2.5	**10** (11%)

[a] $Pd(OAc)_2$ (1.0 equiv.); [b] $Pd(OAc)_2$ (2.4 equiv.); [c] additive (5.0 equiv.)

The proposed mechanism of Pd-promoted dehydrogenation-cyclization reaction:




(B)
TMSOTf (3 equiv)
NEt3 (3.5 equiv)
THF, -78 °C
t-BuO2Li (3.9 equiv)
THF, -10 °C
(60%)
DMP (5 equiv)
DCM, 0 °C
H2SO4
(0.8 M)
MeCN
35 °C
Me3OBF4 (5 equiv)
DCM, 26 °C
then H2O
TMSCHN2, 0 °C
(3 steps 41%)
NaBH4 (1 equiv)
EtOH/DCM
-10 °C
(68%)
21
22
22'
23
24
25
viridin (1)
viridiol (4)


ButOOLi
+
O
OR1
R2
Li
O
OR1
ButO
R2
O
OR1
Li
O
ButO
H
R2
O
OR1
O
H
R2

谢谢